Case Report

A Case of Severe Primary Hyperthyroidism, Secondary Hyperparathyroidism, Adrenal Insufficiency and Osteoporosis with Multiple Fractures

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ABSTRACT

Osteoporosis is generally known to be one of the most serious adverse effects of long-term corticosteroid administration. Recently it was discovered that corticosteroid-induced osteoporosis occurs not only in trabecular bone but also in cortical bone, leading to the reduction in the strength of bones and subsequent fracture. We report a case of severe hyperthyroidism, secondary hyperparathyroidism, adrenal insufficiency and osteoporosis with multiple fractures (most likely collectively due to chronic steroid intake because of steroid dependant bronchial asthma, hyperparathyroidism and hyperthyroidism) which was treated appropriately and made an uneventful recovery.

KEY WORDS: corticosteroid therapy, hyperparathyroidism, hyperthyroidism, osteoporosis

CASE HISTORY

This 26-year-old female, married, having regular menstruation, was a known asthmatic on prednisolone 10 mg daily for about 10 years. She was admitted in the medical department of King Khaled General Hospital, KSA with suspected deep vein thrombosis (DVT). In the course of her investigation DVT was ruled out but she was found to have severe hyperthyroidism though clinically mildly symptomatic. She had severe osteopenia with multiple pathological fractures with sign of healing over the shaft of both fibulae and femur bilaterally, detected on plain X-ray (Fig. 1 and Fig. 2).

Examination revealed a conscious and oriented patient. Pulse and BP were 120 / min and 90/60 mmHg respectively. She had mild diffuse goiter without bruit, fine tremor and no ophthalmopathy or pre-tibial myxedema. The proximal muscles were weak with tenderness in thigh muscles on both sides. She could barely stand with support and hence postural drop of blood pressure could not be assessed. Other systemic examination revealed no significant abnormalities. Laboratory evaluation depicted that she had primary hyperthyroidism as her FT$_3$ was 30.19 pmol/l (N = 2.8 – 7.1 pmol/l), FT$_4$ 57.70 pmol/L (N = 12 – 22 pmol/l), and TSH 0.006 µU/ml (N = 0.27 - 4.2 µU/ml). Secondary hyperparathyroidism was diagnosed...

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as her Ca was 7.4 mg% (N = 8 - 10.5 mg%) and PTH 152 pg/ml (upper limit 62 pg/ml) with PO$_4$ 2.3 mg% (N = 2.5 - 5 mg%), alkaline phosphatase 378 U/l (N = 40 - 230 U/l) and normal albumin. Secondary adrenal insufficiency was diagnosed as her cortisol was low, 165.17 nmol/l (N ≥ 550 nmol/l) one hour after ACTH stimulation with normal electrolytes. Level of 25-hydroxy vitamin D and 1, 25-dihydroxy vitamin D were also normal. She had severe osteoporosis as revealed by DEXA (T score = -3). Other investigations showed normal CBC, mild microcytic hypochromic anemia with normal ESR, renal and hepatic functions. Doppler sonography of the left leg was normal. The ultrasonography of thyroid showed right lobe 6 x 1.4 x 3 mm and left lobe 6.9 x 1.7 x 2.2 mm with no focal lesion. The plain X-ray of bilateral fibulae and femur revealed multiple healing fractures. ECG showed sinus tachycardia.

The patient was managed conservatively by the orthopedic team. She was started on alendronate 70 mg weekly, alfacalcidol 1 µg daily and calcium carbonate (CaCO$_3$) 600 mg thrice a day. Her fractures healed completely within four months. Initially, her heart rate was controlled by propranolol without compromising her asthmatic state under the coverage of steroid which was discontinued eventually. She was also subjected to propylthiouracil therapy for hyperthyroidism. The follow up after six months revealed her to be in euthyroid state clinically and biochemically with controlled asthma.

**DISCUSSION**

Osteoporosis represents a major and emerging public health problem with the aging population. Major clinical consequences and economic burden of the disease pertain to the ensuing fractures. Many risk factors are associated with these fractures including low bone mass, hormonal disorders namely hyperparathyroidism and hyperthyroidism, thin built, use of certain drugs (e.g., glucocorticoids), cigarette smoking, excessive intake of alcohol, low physical activity, vitamin D insufficiency and low intake of calcium[7]. Osteoporosis and thyroid dysfunction are both common in older women. Eight to 13% of women older than 50 years of age have biochemical evidence of thyroid dysfunction and 30% are osteoporotic according to the bone density criteria[9]. The osteoporotic fractures have long been associated with florid hyperthyroidism[10] although the relationship between biochemical evidence of excess thyroid hormone and fracture risk is not known[11]. The risk for hip fracture is more than threefold and that of nonspine fracture is twofold higher among women with low TSH levels than those with normal TSH levels[12]. Biochemical markers of bone turnover are elevated in women with low TSH levels supporting the view that low TSH levels reflect excessive thyroid hormone, which in turn increases skeletal remodeling[12]. All patients with hyperparathyroid disease will eventually develop osteoporosis regardless of their age or sex. Women tend to develop osteoporosis from parathyroid disease faster than men[13]. Osteoporosis is a well-recognized

![Fig. 1: X-ray showing fracture of the both femurs with signs of healing](image1)

![Fig. 2: X-ray showing fracture of the right fibula with signs of healing](image2)
adverse effect of corticosteroid therapy. The bone loss is most marked during the first six to 12 months of treatment. Corticosteroids affect both bone formation and bone resorption. A decrease in bone formation has been attributed to a decrease in osteoblast activity, number and life span (apoptosis). Corticosteroids alter gonadal sex steroid production through straight action and inhibition of gonadotrophin secretion and suppress adrenal androgen production, resulting in decreased bone formation[14]. They also increase the rate of bone resorption by stimulating the formation and action of osteoclasts[15]. The increase in bone resorption also may be explained, in part, by increased parathyroid hormone (PTH) mediated activation of osteoclasts having PTH receptors which osteoclasts are lacking. PTH-mediated stimulation of osteoclasts is believed to be indirect, acting in part through cytokines released from osteoclasts to activate them[16]. The secondary hyperparathyroidism results from reduced intestinal as well as renal tubular calcium absorption by steroid[17].

Patient receiving glucocorticoids chronically may have depressed circulating level of 1, 25 dihydroxy vitamin D; the mechanism being unknown[18]. However, other studies show no consistent abnormalities in vitamin D, PTH, or calcitonin levels in glucocorticoid-treated patients[19]. Common osteoporotic fracture sites include the vertebrae, the hip, the distal radius of the forearm with an incidence of 32, 16 and 15 percent respectively[20]. Osteoporotic bones are ten times more susceptible to fracture than normal[21] which often does not become clinically apparent until a fracture occurs. The best screening test is dual energy X-ray absorptiometry (DEXA) which is quick, simple and precise. It measures the density of bones in the areas most likely to be affected and accurately follows the changes in these bones over time[22]. Recently, many studies showed the need to administer vitamin D 800 IU or alfacalcidol 1 µg or calcitriol 0.5 µg/day in treatment of osteoporosis. Active vitamin D analogues, such as calcitriol and alfacalcidol, stimulate the formation and action of osteoclasts[23] leading to increased bone formation[24]. Effects of vitamin D resulted in lower risk of fractures and falls, as well as improvement of neuromuscular performances. In more than ten years of practice and several short and long term clinical studies, alendronate 70 mg/week lowered the risk of vertebral and extra-vertebral fractures and improved bone mineral density (BMD) of all measured sites in both sexes with osteoporosis. The positive results of alendronate were demonstrated in different entities like persons of various ages and grades of lower BMD or patients with glucocorticoid-induced osteoporosis. Combination of vitamin D with efficacious antiresorptive drug like alendronate maintains all pharmacological features and demonstrates the clinical effects of weekly alendronate[25]. PTH analogue seems superior in prevention of vertebral fractures although their long term safety needs to be established.

We report a case of severe primary hyperthyroidism, secondary hyperparathyroidism, adrenal insufficiency, and osteoporosis with multiple fractures, most likely due to chronic steroid intake because of steroid dependent bronchial asthma. Secondary hyperparathyroidism in our patient may be explained by hypocalcemia resulting from decreased intestinal absorption and increase renal excretion of calcium due to decreased tubular reabsorption by steroid. Adrenal insufficiency resulted from chronic steroid administration.

CONCLUSION

The atypical presentation (uncommon early age - osteoporosis and unusual site of fracture) is probably multifactorial. The treatment was directed towards the etiology and consequences of the diseases, leading to uneventful recovery. In such a patient presenting with osteoporosis even with subtle symptoms of thyrotoxicosis, thyroid hormonal evaluation is warranted. Furthermore, parathyroid hormone assay is indeed one of the most important biochemical markers in an osteoporotic subject.

REFERENCES


